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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/973,363	02/04/98	GRIFFITHS R	263PPNTIR117

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EXAMINER	
SCHNIZER, R	
ART UNIT	**PAPER NUMBER**
1632	18

DATE MAILED: 10/04/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

[redacted]

FILE COPY

Office Action Summary	Application No. 08/973,363	Applicant(s) Griffiths
	Examiner Richard Schnizer	Group Art Unit 1632

☐ Responsive to communication(s) filed on _____

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *34-54* is/are pending in the applicat

Of the above, claim(s) *50-54* is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *34-49* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☒ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☒ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☒ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

An amendment was received and entered as Paper No. 17 on 7/3/00.

Election/Restriction

Applicant has requested reconsideration of the restriction requirement in light of arguments that the restriction was improper under PCT practice because the claims do not lack unity of invention. Specifically, applicant argues that the polypeptides of claims 50-52 have unity with the nucleic acids because they are encoded by the nucleic acids. This is unconvincing because the use of the nucleic acids does not depend upon the expression of the proteins. The nucleic acids can be used in hybridization or PCR assays to determine the sex of birds. The functions of the encoded proteins are unknown, thus one cannot use them for any purpose involving their activity. One may argue that the encoded proteins could be used for sex-determination by raising antibodies against them, however, this represents a patentably distinct endeavor which does not necessarily require the claimed nucleic acids. Applicant also argues that the antibodies have unity of invention with the nucleic acids because they are products of the nucleic acids. The claimed antibodies are not the product of the claimed nucleic acids. The claimed nucleic acids do not encode antibodies, and are not required for the synthesis of the claimed antibodies. One might argue that the nucleic acids and antibodies are related as intermediate and final products. This argument would be invalid because nucleic acids and antibodies lack any similar structural element. For these reasons finality of the restriction requirement is maintained. Finally, 37 C.F.R 1.475(b) does not provide for multiple independent products, and the claimed nucleic acids, proteins, and antibodies are all distinct products having

different structures and functions. Claims 50-54 are withdrawn from consideration. Claims 34-49 are under consideration in this office action.

The allowability of claims 34 and 35, indicated in Paper No. 15, has been withdrawn in view of the following new grounds of rejection.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 34-49 rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for isolated nucleotide sequences consisting of SEQ ID NOS: 1, 2, 3, 4, 5, 10, 12, 13, or 15, does not reasonably provide enablement for any other nucleic acid. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 34-41 are drawn to a broad genus of nucleic acids, some of which would not be expected to hybridize to W-specific sequences under any circumstances. The claims recite fragments of nucleotide sequences, wherein the nucleotide sequences **comprise** nucleotide sequences according to SEQ ID NOS: 1-5, 10, 12, 13, or 15. Thus the claims are drawn to

sequences which are not necessarily related to CHD-W sequences at all. For example, plasmid DNA comprising SEQ ID NO:1 is encompassed by the claim. Plasmids routinely comprise such sequences as including antibiotic resistance genes, origins of replication, and polylinkers. One of skill in the art would not reasonably expect that a fragment of a plasmid antibiotic resistance gene would give a W-specific signal when hybridized to non-ratite bird genomic DNA.

With respect to claims 35, 37, 39, 41, 43, 45, 47, and 49, the invention comprises nucleic acid sequences which comprise nucleic acids encoding the polypeptide sequences of SEQ ID NOS: 6-9, 11, and 14 which give a W-specific signal upon hybridization to nucleic acids from any non-ratite bird. These nucleic acids correspond to degenerate forms of sequences encompassed by claim 35.

Hybridization between two nucleic acids can be thought of as occurring between a probe sequence and a target sequence. Applicant has described the amino acid sequences of SEQ ID NOS: 6-9, 11, and 14, and it is well within the ability of one of skill in the art to determine all of the nucleic acid sequences which could encode these amino acid sequences. Thus Applicant has taught a wide variety of probe sequences. However, Applicant has not taught which of these sequences can be used in the invention. For example, if one were to make a probe by changing every wobble base in SEQ ID NO:2, which encodes a mouse CHD-1 gene, the resulting probe sequence would be about 67% identical to SEQ ID NO:2 and would be encompassed by the claims. SEQ ID NO:2 is about 80% identical to the chicken CHD-1A gene, and CHD-1A is about 90% identical to CHD-W. See page 23, lines 5 and 6, and page 25, lines 19-21. Thus it seems reasonable that the probe would be about 50% identical to the W-specific CHD-W target

sequence. Under the hybridization conditions disclosed at page 9, lines 13-16 of the specification, one would not expect such a probe to hybridize to the target sequence at all. Furthermore, Applicant has not taught any target sequence other than chicken and great tit sequences, and there appears to be no guidance in the prior art as to the sequence of any target nucleic acids not disclosed in the specification. Thus there appears to be no way to accurately predict which of the described probes will be useful for generating a W-specific sequence in birds other than the chicken or the great tit. For these reasons, one of skill in the art would be unable to select appropriate probes from the described genus, and would be unable to use the claimed sequences invention commensurate in scope with the claims without undue experimentation.

Claims 48 and 49 are specifically drawn to a method of determining the sex of a non-ratite bird by hybridization of the nucleic acids of claims 34, 35, 42, or 43 to RNA isolated from the bird. The claimed nucleic acids are homologous to the CHD-1A and CHD-W genes which Applicant has shown to be conserved in at least 13 species of widely disparate birds. Both genes are transcribed into RNA, however the specification does not appear to teach how to distinguish between the RNAs transcribed from these two genes. No information is presented with respect to differences in the sizes or tissue distribution of the two classes of RNAs, so it is unclear how any claimed nucleic acid could be made or used to provide a W-specific signal could be generated by hybridization with the claimed sequences.

The specification provides convincing evidence that SEQ ID NOS: 1-5, 10, 12, 13, and 15 can be used to yield a W-specific signal when the DNAs of the subject bird have been digested with the restriction enzyme DdeI. Digestion with Dde I is performed because the claimed nucleic

acids hybridize to both autosomal-specific (CHD-1A) and W-specific (CHD-W) avian sequences, thus some method of differentiating between CHD-1A and CHD-W signals is required. For example, the specification teaches that PCR amplification of genomic DNA from a variety of birds gives fragments of precisely the same length which correspond to both CHD-1A and CHD-W sequences. Digestion with a restriction endonuclease which recognizes CHD-W nucleic acids allows one to distinguish the CHD-W signal from the CHD-1A signal. The specification teaches no method other than restriction digestion which can be used to distinguish these signals. For this reason, the claimed nucleic acids could not be used to provide a W-specific signal when applied to non-condensed chromosomal DNA *in situ*, or to DNA which has not been, or will not be, digested with a restriction endonuclease that allows separation of fragments of diagnostic sizes. Furthermore, one of skill in the art could not make any claimed sequence which could be used to do so.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 36-41 and 44-47 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 36-41 and 44-47 are indefinite because it is unclear what is intended by the term "W-specific" in the context of sequences which give rise to W-specific hybridization signals.

Taken literally, this term appears to refer to any signal which originates from the W-chromosome. Thus a random hexamer nucleic acid, which hybridizes to all chromosomes at thousands of sites, could be interpreted as giving a variety of W-specific signals in addition to other signals which are not W-specific. Such a nucleic acid would anticipate the claim. Alternatively, the term could refer to a nucleic acid which hybridizes only to the W-chromosome, and not to any autosomes. Finally the term could be interpreted as referring to a pattern of signals, or a fingerprint, which is diagnostic of the W-chromosome. Clarification is required.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 36-47 are rejected under 35 U.S.C. 102(b) as being anticipated by Delmas et al (Proc. Nat Acad. Sci USA 90(6): 2414-2418, 1993).

Delmas teaches a single polynucleotide with 66.7% homology to SEQ ID No. 2 and 67.2% homology to SEQ ID No.15. In the absence of evidence to the contrary, this polynucleotide is deemed to be able to specifically hybridize under moderate to high stringency conditions to sequences comprised by SEQ ID Nos. 2 and 15. See Fig 1, page 2415. Because the sequence of Delmas comprises segments of 100% identity with those of SEQ ID Nos. 2-5, 10,

and 15, it is deemed to comprise fragments of nucleotides sequences according to claims 34 and 35, thus claims 36 and 37 are included in this rejection. The specification does not explicitly preclude a "fragment" from being physically associated with other less homologous sequences. Thus the regions of highest homology within the Delmas sequence can be construed as fragments which anticipate the claim. Claims 38 and 39 are product by process claims in which the process of restriction endonuclease digestion is accorded no patentable weight. Thus Delmas anticipates the claims.

Claims 36-41 are rejected under 35 U.S.C. 102(b) as being anticipated by random hexameric nucleic acids, product C1181 in the 1990/1991 Promega Biological Research Products Catalog, page 138.

The Promega Biological Research Products Catalog teaches random hexamer nucleic acids. This mixture of nucleic acids comprises all possible combinations of nucleic acid hexamers, therefore the mixture comprises oligonucleotides which will hybridize to any single stranded nucleic acid. For this reason, the random hexamers can give rise to a variety of signals by hybridizing to the W-chromosome. These signals can be thought of as W-specific because they originate at the W-chromosome.

Thus random hexanucletides anticipate the claims.

Response to Arguments

Applicant's arguments filed 7/3/00 have been fully considered but they are not persuasive.

Applicant argues that the sequence of Delmas will not hybridize with the claimed sequences under the conditions recited in the specification. Specifically applicant states that the scope of the claim encompasses nucleic acids of "at least about 75% homology". The specification at page 9, line 14 says that moderate stringency conditions correspond to "about 75% homology". Clearly 75% is not set forth as a minimum value, and the word "about" allows for sequences of less than 75% identity. Applicant has presented no evidence which suggests that the sequence of Delmas will not hybridize with SEQ ID NO:15 with which it is 67.2% homologous under the recited conditions, so the rejection is maintained. Furthermore, Delmas teaches sequence fragments of greater than 75% identity to SEQ ID NO:15 merely by presenting the DNA sequence of Fig. 1 on page 2415. This sequence was determined by dideoxy chain termination sequencing. This procedure involves separating nucleic acids of between approximately 30-500 bases in length on polyacrylamide gels. The sequence of Delmas was determined by generating thousands of these overlapping polynucleotides, so most of the bases in the sequence represent a polynucleotide of between about 30 and 500 bases. The first 540 bases of SEQ ID NO:15 are 79% identical to bases 3757-4296 of Delmas (115 mismatches/540 bases). Thus, the overwhelming likelihood is that the sequence of Delmas discloses hundreds of discrete polynucleotides which are at least 79% identical to portions of SEQ ID NO:15. Absent evidence to the contrary, these sequences anticipate the claims.

Applicant also argues that the specification positively disclaims all sequences which were known in the prior art. For the purposes of examination under 35 U.S.C.102 and 103, the relevant consideration is whether or not the claims embrace the prior art. Any disclaimer in the

specification is not relevant to the analysis. If Applicant wishes to exclude the sequence of Delmas from the invention, then this must be explicitly stated in the claims. However, such an amendment would constitute new matter if there is no literal support for it in the specification.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 703-306-5441. The examiner can normally be reached on Mondays and Thursdays between the hours of 6:20 AM and 3:50 PM, and on Tuesdays, Wednesdays and Fridays between the hours of 7:00 AM and 4:30 PM (Eastern time). The examiner is off every other Friday, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Karen Hauda, can be reached at 703-305-6608. The FAX phone numbers for art unit 1632 are 703-308-4242 and 703-305-3014.

Inquiries of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is 703-308-0196.

Karen M. Hauda

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